HISTOLOGY OF OVARIES

The female reproductive system consists of

- **Paired ovaries.**
- **Paired uterine tubes (fallopian tubes or oviducts).**
- **The uterus.**
- **The vagina.**
- **The external genitalia which consist of (clitoris, labia majora and labia minora)**

OVARIES

Functions: (mixed exocrine and endocrine gland)

- Production and maturation of the female **germ cells or the ova (exocrine function).**
- Production of the **female sex hormones; estrogen and progesterone (endocrine function).**
- They are the ones that consist of **paired almond-shaped glands** approximately 3 x1.5 x 1 cm and located **intraperitoneally.**

Histological structure of ovary

1.Surface

- It is covered by **simple squamous or low cuboidal epithelium** called "**germinal epithelium**" but it is not germinal.
- **Tunica albuginea** is a layer of connective tissue mainly collagen fibers present **under germinal epithelium** and is responsible for the whitish color of the ovary.

2. Cortex

- It is present **under the tunica albuginea** where ovarian follicles at different stages of maturation are found.
- The follicles are **embedded in the connective tissue (stroma).**
- Cortical stroma is characterized by the presence of spindle shaped fibroblasts that respond to hormonal stimuli.

3. Medulla:

- It is the **most inner part** of the ovary
- The medullary stroma consists of loose fibroelastic connective tissue.
- It contains rich vascular bed, lymphatics and nerves within the stroma.
- **Hillar cells** are present in the hilum & they are **similar to Leydig cells** of the testis (secrete androgens).
- **NB.** There is **no clear line** of demarcation between cortex and medulla.

The ovarian follicles include

1. **Primordial follicles**
2. **Unilaminar primary follicle**
3. **Multilaminar Primary follicles**
4. **Secondary (growing) follicles**
5. **Mature (Graafian) follicles**
6. **Atretic follicles**

[1] PRIMORDIAL FOLLICLES

- They start to appear during the **intrauterine life** in the cortex.
- Each follicle consists of a **primary oocyte** surrounded by **a single layer of flattened follicular cells**.
- The follicular cells are separated from the surrounding stroma by a **prominent basal lamina**.
- The oocyte in the primordial follicle is present in the prophase of the first meiosis.
- **Structure of primary oocyte**
  - Spherical in about **25 µm**.
  - Contains a large eccentric nucleus with prominent nucleolus.
  - Its cytoplasm contains mitochondria, Golgi complexes, RER and annulate lamellae.
- **N.B:** At the time of puberty, follicular growth is stimulated by follicle-stimulating hormone **(FSH)** secreted by the adenohypophysis and the unilaminar follicles appear.

[2] UNILAMINAR PRIMARY FOLLICLE

- The follicular cells form **a single layer (unilaminar) of cuboidal cells** around the primary oocyte.
- The primary oocyte increases in size to become **50 Mm** in diameter.
- The oocyte is surrounded by an amorphous material of glycoprotein called **zona pellucida** (synthesized by oocyte and follicular cells) separating it from the follicular cells.
- Microvilli from the oocyte and cytoplasmic processes from the follicular cells invade the zona pellucida.

[3] MULTILAMINAR PRIMARY FOLLICLE

- The follicular cells proliferate, form a **stratified follicular epithelium (multilaminar)** called **granulosa cells**, and communicate through numerous gap junctions.
- The stromal cells around the follicle become closely packed and **form theca folliculi**
- **Fluid (liquor folliculi)** secreted by follicular cells begin to accumulate between the follicular cells.
- The small cavities that contain this fluid coalesce & form a **single cavity (antrum).**
- The primary oocyte is present inside a mass of granulosa cells that arrange and protrudes toward the interior of the antrum **(cumulus oophorous).**

[4] SECONDARY (GROWING) FOLLICLE

- The primary oocyte increases in size to reach a diameter of **125 Mm**.
- The primary follicle increases in size **(200 Mm)** due to increase in the size & number of granulosa cells .
- The granulosa cells proliferate forming many layers (6-10) around the oocyte that is displaced to one side
- The layer of granulosa cells that in contact with the zona pellucida, becomes tall and is called **corona radiata.**
- There is a thick basement membrane between theca folliculi and granulosa cells.
- The theca folliculi differentiates to form two layers:
  1. **Theca externa** consists of layers of fibroblasts and collagen fibers with many blood vessels in between.
  2. **Theca interna**
- It is formed of several layers of rounded cells that secrete the precursor of estrogen hormone.
- The cells have the ultrastructure character of **steroids secreting cells** as abundant sER, mitochondria with tubular cristae, and numerous lipid droplets.
- It is rich in capillary plexus around the secretory cells.

[5] MATURE (GRAAFIAN) FOLLICLE

- Only one follicle which grows much more than the others and becomes the dominant follicle during menstrual cycle (other follicles enter atresia).
- It increases in size to about 2 cm in diameter, protrudes from the surface of the ovary, and can be detectable with ultrasound (sonar).
- It has the same histological structure as the secondary follicle, but the antrum increases in size due to accumulation of more
- A primordial follicle needs 10-14 days to reach maturity.

[6] FOLLICULAR ATRESIA

- The ovaries of young female contain about **600,000** follicles and **only less than 500** develop to mature follicles.
- The remaining follicles undergo follicular atresia.
- More than **99%** of ovarian follicles (primordial, primary, secondary and mature) may undergo degenerative changes called atretic follicle.
- Follicular atresia **starts after birth and continues a few years after menopause**.
- Atresia is greatly accentuated in the following periods:
    1. **Just after birth** because the effect of maternal hormones subsides.
    2. **During puberty and pregnancy** because marked hormonal variations take place.
- These follicles are phagocytosed by phagocytic cells.
- Atretic process is characterized by:
    1. **Termination of mitosis** in the granulosa cells.
    2. **Detachment of granulosa cells** from the basal lamina which undergoes **hyalinization** (called **glassy membrane)**
    3. **Death** of the oocyte.
    4. **Invasion of macrophages** to phagocytose the debris.
    5. Fibroblasts produce a **scar of collagen fibers.**
    6. The **theca interna cells** persist in small groups in the cortical stroma that are called **interstitial cells**. These cells are active **steroid secretors stimulated by LH**.

Ovulation

- Ovulation is the process by which the **mature follicles rupture** with the release of the secondary oocyte.
- Ovulation takes place at the **middle of the menstrual cycle** i.e. in human around the **14th day** of a 28-day cycle.
- **Formation**

1. The anterior pituitary gland secretes a **surge LH** in response to high levels of circulating estrogen produced by the growing follicles.
2. Blood flow increases in the ovary, **resulting in edema.**
3. The granulose cells produce more **hyaluronic acid** resulting in an **increased pressure** of the liquor folliculi.
4. A local release of **prostaglandins, histamine, vasopressin, and collagenase**.
5. A small area of the wall of the follicle becomes weak and semi-transparent (stigma)
6. The oocyte continues its first meiotic division **shortly before ovulation** to produce secondary oocyte (1n&2c) and first polar body
7. Degradation of the tunica albuginea and rupture of the outer follicular wall resulting in release of secondary oocyte, first polar body (minimal amount of cytoplasm) and liquor folliculi.
8. The secondary oocyte (1n & 2c) enters the second meiotic division **to arrest in metaphase** until **fertilization**

NB

- Usually, one oocyte is liberated during each cycle, but sometimes **no oocyte is ovulated** (un ovulatory cycle).
- Sometimes **2 or more oocytes** are expelled at the same time, and if they are fertilized, there may be **2 or more fetuses**.
- If fertilization does not happen within the **first 24 hours** after ovulation, 2ry oocyte degenerates and is phagocytosed.

Corpus luteum

- After ovulation, the high level of **LH stimulates** reorganization of the remainder of the ovulated follicle and development of a **temporary endocrine gland** called **corpus luteum (yellow body)**.
- Formation of Corpus Luteum
  1. Release of the liquor folliculi results in **collapse of wall of the graafian follicle** so that it becomes folded.
  2. Some blood flows into its cavity.
  3. It coagulates and forms a blood clot **(corpus haemorrhagicum).**
  4. Later this clot is **removed by phagocytes** and invaded by connective tissue that remains at the center of the corpus luteum.
  5. Under the **effect of LH:** the granulosa cells are modified into **granulosa lutein cells** with the characteristics of steroid-secreting cells **(secrete progesterone).**
  6. The theca interna cells give rise to **theca lutein cells (secrete estrogen)** that inhibits further release of **gonadotropin–releasing hormone (GnRH)** and thus secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

Fate and types of corpus luteum

1. Corpus luteum of menstruation: after ovulation, the elevated level of LH allows the corpus luteum to secrete estrogen and progesterone for 10-12 days.

2. Corpus luteum of pregnancy: If pregnancy occurs, trophoblasts of implanting embryo synthesize human chorionic gonadotropin hormone **(HCG)** that prevents degeneration of corpus luteum and stimulates its further growth and persistence during the **first 3 months of pregnancy**.

3. Corpus albicans: If pregnancy does not occur,

- ✓ No further hormonal stimulation takes place
- ✓ The cells of the corpus luteum degenerate by apoptosis.
- ✓ Its cellular remnants are phagocytosed by macrophages.
- ✓ Neighboring fibroblasts invade the area and produce a scar of dense connective tissue called **corpus albicans**.